

# Letters to the Editor . . .

## SOVIET "ACS" THERAPY

In 1900, Metchnikoff<sup>3</sup>, applying the pharmacological principle that small doses of toxic drugs may stimulate rather than damage, expressed the idea that stimulation of tissues could be accomplished by the employment of small doses of antiserum specific for these tissues. Twenty-four years later, one of his students, Bogomolets<sup>1</sup>, and his colleagues of the Ukraine, began a study of the possibility of stimulating the physiological activity of connective tissues by the injection of small doses of species-specific antireticular cytotoxic serum ("ACS").

Since then, numerous experimental and clinical successes have been reported by Soviet investigators. Among these, Varchamov<sup>6</sup> reported stimulation of the production of antishock hemolysins and *B. Typhosus* agglutinins in rabbits. Neuman<sup>4</sup> reported the saving of 75 per cent of mice infected with recurrent typhus, whereas 100 per cent of the controls died. Others<sup>1</sup> reported increased rate of healing of experimentally produced fractures in rabbits, decreased number of takes and reduced number of metastases in transplanted cancer in mice. Clinically there was found to be an accelerated healing of severe frostbites, gangrene and war wounds, together with favorable effects in early stages of hypertension, "acute rheumatism," polyarthritis, pulmonary abscess, and tuberculosis.

In view of the numerous and remarkable claims thus made, a feeling of skepticism is natural. Because of its potential importance, however, the claims of therapeutic effects of "ACS" are worthy of attempted confirmation. This has been undertaken by Straus<sup>5</sup> and his associates of the Cedars of Lebanon Hospital, Los Angeles, California.

In their initial study, anti-human "ACS" was prepared by a slight modification of the Soviet technic.<sup>2</sup> Emulsified spleen and bone marrow from fresh human cadavers were extracted for 30 minutes at room temperature in five volumes of saline solution. After centrifugation the supernatant fluid was injected intravenously at three-day intervals in progressively increasing doses into young rabbits. Five to seven days after the sixth injection the animals were bled by cardiac puncture. The resulting antisera were titrated by the complement-fixation reaction. At this time the titers usually varied from 2,500 to 10,000 arbitrary units.

Anti-rabbit "ACS" was prepared by the same technique, by injecting rabbit spleen and bone marrow extracts into young goats. Both the anti-human and anti-rabbit ACS were species-specific, giving negligible cross-reactions. In the undiluted state both sera may be kept at 4°C or at room temperature for a year or more with but slight deterioration. After dilution with saline solution both sera deteriorate rapidly.

The Soviet investigators claim that intravenous injection of large doses of homologous "ACS" inhibits or prevents normal healing of bone fractures; but that small doses of the same antireticular serum have the opposite effect, causing accelerated or more perfect healing. To test this claim, experimental fractures were made, under nembutal anesthesia, of the right radius and ulna of 256 healthy

female rabbits, each weighing 2.25-2.50 kg. The fractures were made by means of a special osteoclast that would secure as much uniformity as possible in the location, orientation, cleanness and completeness of the fractures. Reduction of the fractures was accomplished immediately without the aid of a fluoroscope. The limbs were then encased in a light cast.

On the third day after the fracture the animals were separated at random into five groups. Each of the animals of group A was injected intravenously with 0.00125 cc. of anti-rabbit "ACS", the recommended "stimulating dose" of the Soviet investigators. Animals of group B were given 0.1 cc. anti-rabbit "ACS", the recommended "depressing" dose. Control groups C and D were given similar injections with normal goat serum. Control group E received no serum.

Roentgenograms were made of the fractured extremities at periodic intervals. On the 14th day the animals were sacrificed and the fractured forelegs stripped of soft tissues. The extent of the healing was estimated by comparing the size and character of the callus and the mobility and strength of the fracture site. The average roentgenographic score, recorded in degrees groups (B), rising to 3.06 for the stimulated group (A). The average strength of the healed fractures was 3.41 kg. for the three control groups (C, D, E.), falling to 0.79 kg. for the "depressed" group (B), and increasing to 6.83 kg. for the "stimulated" group (A). Stimulating doses of "ACS" thus doubled the rate of normal healing of experimental fractures. Toxic doses of the same serum decreased the rate of healing to about one-fourth normal. Histological studies confirmed these differences.

The California investigators have thus confirmed the Soviet claims that small doses of homologous "ACS" accelerate connective tissue proliferation. This confirmation may go far to decrease the current skepticism of the Soviet clinical claims. The alleged acceleration of antibody production by ACS stimulation of the reticulo-endothelial system is of particular theoretical and clinical interest. This claim is now under investigation.

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## REFERENCES

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